FACTSHEET

SAFE DRINKING WATER PROGRAM

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National Toxicology Program

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NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

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The introduction of chlorination of drinking water supplies as a standard treatment has greatly decreased mortality from infectious disease and was a major public health advance in the 20th century. However, chemical contaminants, both those associated with the disinfection process (disinfection by-products, DBP) and those occurring naturally or by contamination in public water systems, may still be present in finished water. The list of known or anticipated unregulated chemicals, in addition to DBPs, found in drinking water (Contaminant Candidate List, CCLs) was published by the US Environmental Protection Agency (EPA) in 1998 in response to a Congressional mandate under the Safe Drinking Water Act Amendments of 1996.

Because of the public health benefits of water disinfection and the fact that more than 200 million Americans use treated drinking water, a critical issue facing water utilities and the EPA is minimizing the potential for chemical-related health effects while still achieving effective control of waterborne microbial pathogens. Determining health risks from exposure to DBPs is a challenge since different disinfection processes result in different DBPs, and the source of water and time of year also influence the presence and relative concentrations of these chemicals. The EPA is expected to set final water standards for DBPs in 2002 or 2003. The National Toxicology Program (NTP) is providing scientific data on those agents that are important for the standard-setting process. Congress also mandated that EPA address potential health risks of drinking water contaminants.

The National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health has substantial expertise in the evaluation of health effects of environmental chemicals and is working through the NTP with EPA on characterizing health risks of DBPs and CCLs. Together the agencies are conducting a systematic, mechanistic-based, toxicological evaluation of DBPs that includes evaluations of reproductive toxicity, immunotoxicity, neurotoxicity, and carcinogenicity. This collaborative effort also involves studies by the Department of Defense (DOD) and interactions with the American Water Works Association Research Foundation (AWWARF); future efforts will involve the extramural research community.

The trihalomethanes are one of the major families of DBPs found in chlorinated water.

- Chloroform, which is the most prevalent trihalomethane, was shown almost 20 years ago to be carcinogenic in rodents. The DOD in collaboration with NTP is evaluating health effects of this chemical in Medaka to determine dose-response relationships in this fish model relative to rodents.
- Bromodichloromethane has also been shown to be carcinogenic in rodents in studies conducted by the NTP and by EPA. Additional NTP drinking water studies will characterize intestinal, renal, and liver responses in rats and mice. Bromodichloromethane is also being studied by the NTP in transgenic mouse models (Tg.AC and p53^{def}) and in the Medaka fish model by DOD.

A second important family of DBPs is the haloacetic acids.

- Dichloroacetic acid and trichloroacetic acid cause liver tumors in mice when given at high concentrations. Dibromoacetic acid, dichloroacetic acid, bromodichloroacetic acid and bromochloroacetic acid are under study by the NTP in short-term rodent studies. Based on results from these studies, several haloacetic acids will be selected for long-term studies and toxicokinetic modeling. Dihalogenated and trihalogenated acetic acids appear to differ in their mechanisms of toxicity, thus members from each family are being considered for long-term studies.
- A long-term study on dibromoacetic acid is in progress and dichloroacetic acid is being evaluated in two transgenic mouse models (Tg.AC and p53^{def}).

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There is very little toxicity data on a third family of DBPs, the haloacetonitriles.

- Dibromoacetonitrile is being evaluated as a representative haloacetonitrile in a long-term rodent study. Additional haloacetonitriles may also be studied depending on the results with dibromoacetonitrile.

Disinfection with chlorine dioxide, a strong oxidant, results in low trihalomethane concentrations in drinking water but high levels of chlorate; toxicity data on chlorate are limited. Studies of chlorate by EPA and NIEHS showed thyroid follicular cell hyperplasia in rats with exposures as short as 21 days. It was proposed that chlorate may interfere with thyroid uptake of iodine.

- Mechanistic studies to explore possible effects of chlorate on the thyroid gland are under way at EPA. An NTP two-year study at doses that cause or do not cause follicular cell hyperplasia is in progress.
- DOD has conducted studies on chlorate in the Medaka model.

Disinfection with ozone, a strong oxidant, produces few DBPs, but bromate is a major by-product of this treatment. Recent EPA studies show that bromate exposure in drinking water causes mesotheliomas in rats and kidney tumors in both rats and mice. Potassium bromate in the feed caused renal cancer in rats.

- Sodium bromate in drinking water has been evaluated by NTP in transgenic mice (Tg.AC and $p53^{def}$).

An interagency agreement between NIEHS and EPA has supported immunotoxicity, reproductive toxicity, and neurotoxicity studies of DBPs. A second Interagency Agreement will support studies on CCLs.

- Immunotoxicity studies on dibromoacetic acid, dichloroacetic acid, sodium bromate chloramine, sodium chlorite and chloroform have been completed.
- A series of reproductive studies of DBPs in rats is being carried out by the NTP in coordination with the two-year bioassays.

NIEHS and EPA scientists are prioritizing toxicology studies on several CCLs, including aluminum complexes, microcystins and organotins, for further evaluation by the NTP.

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Suggested Reading:

1. Dunnick JK and Melnick RL. Assessment of the carcinogenic potential of chlorinated water: experimental studies of chlorine, chloramine, and trihalomethanes. J Natl Cancer Inst. 85:817-822, 1993.

2. Melnick RL, Boorman GA, and Dellarco V. Water chlorination, 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone (MX), and potential cancer risk. J Natl Cancer Inst. 89:832-833, 1997.

3. Boorman GA, Dellarco, V, Dunnick JK, Chapin RE, Hunter, S, Hauchman F, Gardner, H, Cox M, and Sills RC. Drinking water disinfection byproducts: review and approach to toxicity evaluation. Environ Health Perspect. 107 Suppl 1:207-217, 1999.